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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/001,039	12/30/1997	DOUGLAS J. JOLLY	1155.005	6098

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EXAMINER	
GUZO, DAVID	
ART UNIT	**PAPER NUMBER**
1636	38

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/001,039	Applicant(s) JOLLY ET AL.
	Examiner David Guzo	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1 136(a) In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b)

Status

1)[·] Responsive to communication(s) filed on *03 September 2002 and 27 December 2002* .

2a)[ ] This action is **FINAL**. 2b)[X] This action is non-final.

3)[ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)[·] Claim(s) *4,5 and 37-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)[·] Claim(s) *37-41* is/are allowed.

6)[·] Claim(s) *4-5 and 42-56* is/are rejected.

7)[ ] Claim(s) _____ is/are objected to.

8)[ ] Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)[ ] The specification is objected to by the Examiner.

10)[X] The drawing(s) filed on *12/30/97* is/are: a)[ ] accepted or b)[X] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)[ ] The proposed drawing correction filed on _____ is: a)[ ] approved b)[ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)[·] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)[ ] All b)[ ] Some * c)[X] None of:

1.[X] Certified copies of the priority documents have been received.

2.[ ] Certified copies of the priority documents have been received in Application No. _____ .

3.[ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) [ ] The translation of the foreign language provisional application has been received.

15)[·] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [X] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) [ ] Interview Summary (PTO-413) Paper No(s). _____ .
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other: .

Detailed Action

Applicants' response to the Office Action (Notice to Comply) mailed 11/19/02 is acknowledged. Applicants' response is persuasive and the Notice to Comply with the sequence rules is withdrawn.

The indicated allowability of claims 42-56 is withdrawn in view of the newly applied rejection under 35 USC 112, 1st paragraph.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pensiero et al. in view of Mulligan et al. and Hermann et al.

This rejection is maintained for reasons of record in the previous Office Action and for reasons cited below.

Applicants traverse this rejection by asserting that the examiner has not established that the parent application of the Pensiero et al. patent provides support for the claims in the Pensiero et al. patent. Applicants also assert that the examiner has used impermissible hindsight to render the instant claims obvious and that the there is no clear and objective evidence that would motivate the skilled artisan to combine the cited references. Applicants assert that Pensiero et al. does not teach high titers of retrovirus vectors and that Hermann et al. does not teach a preparation of retroviral vectors having a titer higher than 10^6 cfu/ml on HT1080 cells. Applicants assert that Hermann et al. teaches methods of preserving retroviral vectors that may have a titer of greater than 10^6 cfu/ml and not the generation of the claimed retroviral preparations. Applicants indicate that in the absence of teachings to perform greater than 10^6 cfu/ml titers on HT1080 cells, the more efficient HT 1080 cell line would not have been obvious to the ordinary skilled artisan. Applicants also assert that combining the teachings of the three cited references would require considerable modification and the exercise of inventive skill by the ordinary skilled artisan.

Applicant's arguments filed 9/3/02 have been fully considered but they are not persuasive. First, the Pensiero et al. patent has a valid 102(e) date of August 17, 1994 for the subject matter

relied upon in the 102(e) rejection. The application 08/291,765 on pages 2- 4 provides support for preparations of retroviral vectors which are capable of infecting human cells and are resistant to inactivation by human serum. Pensiero et al. contemplates expression of Factor VIII (page 4 of the 08/291,765 application) using the human serum inactivation resistant retroviral vectors. It is noted that the examiner would not have made the 102(e) rejection of claim 4 over the Pensiero et al. patent without checking the 08/291,765 application for support.

Second, contrary to applicants' assertions, Pensiero et al. does disclose high titers of retroviral vectors. For example, in column 21, Pensiero et al. discloses that cell line CAK8 produces recombinant retroviral vectors at titers in excess of 10^6/ml.

Third, since Pensiero et al. teaches that human serum inactivation resistant retroviral vector titers of in excess of 10^6/ml can be obtained, it must be assumed, absent evidence to the contrary, that these titers would be the same using a well known human cell line (HT 1080 cells) previously utilized for assaying titers of recombinant retroviral vectors (as taught by Hermann et al.). Also, contrary to applicants' assertions, the Hermann et al. patent is not being used by the examiner to provide teachings on the generation of retroviral vector preparations at the recited titer level, but instead is being used to show that human HT 1080 cells were previously used to assay the titers of retroviral vector preparations.

Fourth, it is noted that the titers of the claimed retroviruses taught by Pensiero et al. are over 10^6 cfu/ml. If applicants are asserting that these titers would not be the same using HT1080

cells in the assay, the burden is on applicants to provide evidence or reasoning that this is the case.

Finally, with regard to applicants' assertion that combining the teachings of the references would require considerable modification and inventive skill, it is noted that Pensiero et al. teaches generation of high titers of retroviral vectors which are human serum resistant and are capable of expressing a well known gene (Factor VIII, as taught by Mulligan et al.). The titers of the vectors are determined by assaying on a cell line previously used to assay the titers of retroviral vectors. It is unclear where the considerable modifications and exercise of inventive skill is required to generate the claimed composition?

In conclusion, it is noted that the claimed invention is not a method for producing and assaying retroviral vectors but instead is a composition claim. The question to be asked is whether Pensiero et al. in view of Mulligan et al. and Hermann et al. teach that human serum resistant retroviral vectors capable of expressing Factor VIII could be generated at the recited titer when said titer is measured on HT 1080 cells. The answer to this question must be yes because Pensiero et al teaches generation of human serum resistant retroviral vector preparations of greater than 10^6 cfu/ml and further teaches that the human Factor VIII gene (disclosed by Mulligan et al. as capable of being expressed using retroviral vectors) can be expressed using these vectors. Absent evidence to the contrary, it must be considered that the titers obtained by Pensiero et al. (greater than 10^6 cfu/ml) would also be obtained using a well known human cell

previously used for assaying titers of retroviral vectors (Hermann et al.). The retroviral vector titers generated by Pensiero et al. inherently have titers of greater than 10^6 cfu/ml.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-5 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-10, 15-16 and 20-21 of copending Application No. 09/190,941. Although the conflicting claims are not identical, they

are not patentably distinct from each other because claims 4-5 are generic to all that is claimed in claims 9-10, 15-16 and 20-21 of copending application 09/190,941. That is, claims 9-10, 15-16 and 20-21 fall entirely within the scope of claims 4-5 or, in other words, claim 4-5 are anticipated by claims 9-10, 15-16 and 20-21. Specifically, claims 4-5 encompass any preparation (pharmaceutical or non-pharmaceutical) of human serum inactivation resistant replication defective recombinant retroviral vectors which are capable of infecting human cells, express human Factor VIII protein (for any length of time) and have titers measured on HT1080 cells of greater than 10^6-10^7 cfu/ml.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim the retroviral vectors pBA-5a, pBA-5b, pBA-5c, pBA8b and pBA9b wherein said vectors express Factor VIII polypeptide sequences. The vectors pBA-5a, pBA-5b

and pBA-5c are essential for generating the other vectors; however, the instant specification does not provide a written description of how to make these vectors. On p. 158 of the instant specification, applicants indicate that "Further details on the construction of pBA-5a pBA-5b and pBA-5c are provided in co-owned U.S. Serial No. 08/721,327 and co-owned application, attorney docket 1147.004, filed May 5, 1997, entitled "Crossless Retroviral Vectors" and which is also hereby incorporated by reference." U.S. Serial No. 08/721,327 is an abandoned file and it is unclear what Serial No. the other application is. Since the information sought to be incorporated by reference to these documents is essential subject matter and the referenced applications have not been issued as a patent or published, applicant is required to amend the disclosure of the referencing application to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by applicant, or a practitioner representing applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application (See MPEP 608/01(p)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-5 are vague in the recitation of the phrase "...has a titer of HT1080 cells on greater than..." 10^6 cfu/ml or greater than 10^7 cfu/ml because titers of viruses are not measured as "titers of HT1080 cells". Redrafting the claims to read on "...has a titer **on** HT1080 cells **of** greater than..." would be remedial.

It is noted that applicants claim, in the Declaration, priority for the PCT applications PCT/US95/16852 and PCT/US97/11784 under 35 USC 119(a)-(d). This priority claim is not granted because applicants have not filed certified copies of these documents. Since it appears that the PCT documents are U.S. PCTs, applicants should claim benefit for these applications under 35 USC 120 rather than 119(a)-(d). If applicants seek to claim benefit for these PCT applications under 35 USC 120, said claim must be made in the Continuing Data section on the first page of the specification.

Claim 37-41 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo

March 8, 2003

DAVID GUZO
PRIMARY EXAMINER